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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/733,387	12/07/2000	Gregory Donoho	LEX-0104-USA	7426

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EXAMINER
LI, RUIXIANG

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1646	15

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Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No. 09/733,387	Applicant(s) DONOHO ET AL.	
	Examiner Ruixiang Li	Art Unit 1646	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 20 March 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1-3 and 6-9*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Continuation of 5. does NOT place the application in condition for allowance because: the rejection of claims 1-3 and 6-9 under 35 U.S.C. 101 and 112, 1st paragraph remains.

I. Claim rejection under 35 U.S.C. § 101
The instant specification fails to to satisfy the utility requirement set forth under 35 U.S.C. § 101 for the following reasons, as well as for the reasons set forth in the previous office actions (Paper No. 9 and Paper No. 13).

Applicants argue that SEQ ID NO: 44 shares 99% percent identity at the amino acid level over the entire length of NM_170776, which has been annotated by different third party scientists as GPR-97. Thus, those skilled in the art would clearly believe that SEQ ID NO: 44 is GPCR (1st paragraph of page 3 of applicants' response). This has been fully considered but is not deemed to be persuasive because the annotation for the published sequence in Genbank is, again, based upon sequence homology and there is no sufficient information which defines unambigously the function of the published sequence. The question is not whether the instant nucleic acid encodes a GPCR, rather, it is what functions and specific and substantial use it has and what an artisan can do with the invention in its currently available form.

Applicants argue that the refences of Bork and Koonin, Ji, and Yan, do not support the Examiner's position in rejecting the claims for lack of a patentalble utility (pages 3 to page 5). This has been fully considered but is not deemed to be persuasive for the following reasons. Bork and Koonin's conclusion' remarks clearly indicates that the potential importance of sequence analysis in extracting functional signal. However, Bork and Koonin do not teach, in any means, that sequence analysis alone can define the biological functions. In fact, Bork and Koonin further teach many proteins are multifunctional, assignment of a single function, which is still common in genome progects, results in loss of information and outright errors (Table 2). As the Examiner stated in the previous office in paper No. 13, while sequence analysis is important, the information provided or "predicted" based upon sequence homology can only be used as guidance in determining functions or activities of a molecule by experiments. Any functions predicted based upon the sequence homology will have to be confirmed ultimately by bench work. Without specifically defining the activities of the GPCR, the present invention does not have a substantial utility in view of a variety of biological functions.

Applicants also argue tht an exact quote from Ji completely undermines the question of asserted utilty based on sequence homology. The Examiner disagrees. The cited statement simply indicates that a substantial degree of amino acid homology is found between members of a particular subfamily. However, two sequences sharing a certain degree homology may not necessarily belong to the same subfamily and share specific functions and uses. Ji also clearly teach there are putative seven transmembrane molecules, which do not appear to be coupled to a G protein. Even if the protein of the present invetnion were a member of the GPCR family, it would still not provide a patantable utility for the claimed invention because it still requires undue experimentation to define the specific biological function and specific use of the present protein or nucleic acid.

Applicants further argue that Yan does not suggest a high level of uncetrainty in assigning function based on sequence, and thus does not support the lack of utility. Specifically, applicants argue that the different receptors bound by the two isofroms of ectodysplasin are related and EDA-A2 receptor was correctly identified as a member of the tumor necrosis factor receptor superfamily based upon solely on sequence similarity. The Examiner notes that while the two receptors bound by the two isofroms of ectodysplasin are related, i.e., belonging to the TNFR superfamily, they have different activities (See, e.g., page 524, column 3) and are distinct receptors. Even the title of the paper clearly states that the two receptors bound by the two isoforms are distinct. The Examiner further notes that while the EDA-A2 receptor was initially identified as a member of the TNFR superfamily solely based on sequence similarity, as applicants argued, the biological functions of the receptor was not identified. In fact, Yan et al. performed undue experimentation to define the ligand and biological activies of the receptor. As taught by Yan, the members of the TNFR superfamily are involved in a number of physiological and pathological response by activating a wide variety of intracellular signaling pathways (beginning of page 523). The EDA-A2 receptor (XEDAR) fails to bind many known ligands of the TNFsuperfamily (1st column of page 524). Therefore, even if sequence analysis could assign a given protein to a protein family, the protein still does not have a substantial utiltiy because the biological function or activity is not defined. Determining such a biological function of the protein would require significant further research, as demonstrated by Yan, which is not allowed undr 35 U.S.C.§ 101.

In addition, applicants continue to argue for the issues of record (Paper No. 11, November 1, 2002). Applicants' arguments have been addressed in the previous office action in Paper No. 13.

II. Claim Rejections Under 35 U. S. C. §112, 1st Paragraph
The Examiner notes that claims 1-3 and 6-9 were rejected under 35 U.S.C. §112, 1st paragraph because the claimed invention is not supported by either a specific, substantial, and credible utility, or a well-established utility. Claim 1, not claims 1-3 and 6-9, as applicants argued (top of page 10), is further rejected for the scope of enablement.

With regard to the lack of written description rejection, Applicants argue that the Action admists that claim 1 in fact does include a conserved structure' and a 'distinguishing feature, "a strech of at least 22 consecutive nucleotides of SEQ ID NO: 43". The Examiner notes that this is incorrect. A strech of at least 22 consecutive nucleotides of SEQ ID NO: 43 is not a conserved structure and a distinguising feature, because such a limitation does not require that the nucleic acid molecules possess any particular biological activity, nor specify at least which 22 consecutive nucleotides of SEQ ID NO: 43 and how the stech of nucleotides is related to their biological functions. Thus, only an isolated nucleic acid molecule comprising SEQ ID NO:43, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

In addition, applicants continue to argue for the issues of record (Paper No. 11, November 1, 2002). Applicants' arguments have been addressed in the previous office action in Paper No. 13.

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